Copper Phosphoramidite Catalyzed Enantioselective Ring-Opening of Oxabicyclic Alkenes

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Copper Phosphoramidite Catalyzed Enantioselective Ring-Opening of Oxabicyclic Alkenes: Remarkable Reversal of Stereocontrol

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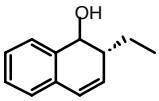
Supporting Information

General: All reactions were conducted in flame dried glassware with magnetic stirring under an atmosphere of argon. Toluene and diethyl ether were distilled from sodium and stored under argon; CH_2Cl_2 was distilled from P_2O_5. Et_2Zn (1.1 M solution in toluene), Me_2Zn (2.0 M solution in toluene), EtMgBr (3.0 M solution in Et_2O), MeMgBr (3.0 M solution in Et_2O), *i*-PrMgCl (2.0 M solution in THF) and *n*-BuMgBr (2.0 M solution in Et_2O) were purchased from Aldrich. *n*-Bu_2Zn (1M in heptane) (Aldrich) was distilled before use and diluted with toluene (1M solution), *i*-Pr_2Zn (1.5 M in toluene) was prepared accordingly common procedures. $Cu(OTf)_2$ (Aldrich) and $Zn(OTf)_2$ (Aldrich) were dried before use.

Analytical TLC were performed on Alugram SIL G/UV254 silica gel sheets (Macherey-Nagel) with detection by 0.5% phosphomolybdic acid solution in 95% EtOH. Silica gel 60 (Macherey-Nagel 230-400 mesh) was used for flash chromatography. Solvents for extraction and chromatography were HPLC grade. Optical rotations were measured on a Perkin-Elmer 241 digital polarimeter with a 1 dm cell. ^{1}H NMR spectra were recorded on a Varian 200 MHz or 300 MHz and on a Brucker AC-200 spectrometers. Chemical shifts are reported in ppm downfield with the solvent resonance, deuterochloroform: δ 7.24. ^{13}C NMR spectra were recorded on a Varian 75 MHz and on a Brucker AC-200 (50MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm downfield with the solvent resonance, deuterochloroform: δ 77.0. Analytical high performance liquid chromatography (HPLC) was performed on a Waters 600E system controller equipped with a Waters 991 photodiode array detector. Enantiomeric excesses were determined by chiral HPLC using Daicel Chiralpak OD or AD columns in comparison with the racemic material. Mass spectra (HRMS) were obtained in an AEI MS-902; infrared spectra (IR) were obtained with a MATTSON 300 FTIR spectrometer.

General procedure for the copper phosphoramidite catalyzed enantioselective ring-opening of oxabicyclic alkenes: A solution of $Cu(OTf)_2$ (10.85 mg, 0.03 mmol) and chiral ligand **2**[1] or **5** (0.07 mmol) in anhydrous toluene (5 ml) was stirred at r.t. for 40 min. The colorless solution was cooled to 0°C followed by subsequent addition of anhydrous $Zn(OTf)_2$ (363 mg, 1.0 mmol) and a solution of *oxabenzonorbornadiene substrate* (1.0 mmol) in toluene (1 ml). After 5 min., R_2Zn (2.0 mmol) was added and the stirred solution was allowed to warm slowly up to r.t. The mixture was quenched with saturated aqueous NH_4Cl solution (1 ml). Extraction with Et_2O and evaporation of the dried ($MgSO_4$) organic phase afforded a crude reaction mixture which was subjected to flash chromatography.

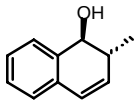
(-)-(*1S, 2R*)-2-Ethyl-1,2-dihydronaphth-1-ol (3a).



The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), substrate **1** (144 mg, 1.0 mmol) and Et_2Zn (1.8 ml); conversion of the starting material (>98%) was reached within 40h. Purification by column chromatography (SiO_2, 15% AcOEt in hexanes) gave **3a** (153 mg, 88%) as a white solid. M.p. = 34°-35°C (uncrist.); R_f = 0.27 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -289.4° (c = 1.26, $CHCl_3$); IR (nujol) 3415, 3025, 2950, 1594, 1384, 1196, 792 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (1H, dd, *J* = 6.6, 1.1 Hz), 7.25-7.15 (2H, m), 7.06 (1H, dd, *J* = 6.6, 1.3 Hz), 6.45 (1H, d, *J* = 9.5 Hz), 5.96 (1H, dd, *J* = 9.5, 4.8 Hz), 4.49 (1H, d, *J* = 4.8 Hz), 2.48-2.39 (1H, m), 1.75 (1H, *OH*), 1.49-1.22 (2H, m), 0.91 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.77, 132.3, 130.7, 128.4, 127.7, 127.6, 126.4, 126.1, 72.1, 43.9, 24.5, 11.5; EI$^+$-MS m/z (relative intensity): 174 (51), 145 (100), 127 (35), 91 (14); Anal. Calcd. for $C_{12}H_{14}O$: C, 82.71, H 8.1, found C, 82.65, H 8.4. The *ee* of 90% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK OD, heptane/*i*-PrOH 99/1, flow: 1 ml/min, λ = 254), retention times were 27.5 min (major) and 32.8 min.

Employing chiral ligand **5** (42.10 mg, 0.07 mmol), substrate **1** (144 mg, 1.0 mmol) and Et_2Zn (1.8 ml), a conversion of the starting material (>98%) was reached within 14h. Purification by column chromatography (SiO_2, 15% AcOEt in hexanes) gave **3a** (160 mg, 92%). The *ee* of 94% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK OD).

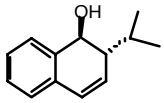
[1] Feringa, B.L.; Pineschi, M.; Arnold, L.A.; Imbos, R.; de Vries, A.H.M. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2620



(-)-(*1S, 2R*)-2-Methyl-1,2-dihydronaphth-1-ol (3b).[2]

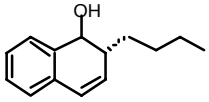
The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), substrate **1** (144 mg, 1.0 mmol) and Me_2Zn (1.0 ml); conversion of the starting material (35%) was reached within 160h. Purification by column chromatography (SiO_2, 15% AcOEt in hexanes) gave **3b** (27 mg, 17%) as a white solid. M.p. = 63°-64°C (uncrist.); R_f = 0.23 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -116.8° (c = 0.61, $CHCl_3$); IR (nujol) 3328, 3038, 1492, 1311, 1195, 788 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (1H, d, *J* = 6.2 Hz), 7.29-7.19 (2H, m), 7.09 (1H, d, *J* = 6.2 Hz), 6.43 (1H, d, J = 9.5 Hz), 5.91 (1H, dd, *J* = 9.5, 4.4 Hz), 4.44 (1H, d, *J* = 5.8 Hz), 2.68-2.56 (1H, m), 1.74 (1H, d, *J* = 5.8 Hz, *OH*), 1.05 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.7, 132.3, 128.3, 127.6, 127.2, 126.4, 125.8, 125.7, 74.1, 37.4, 16.9; EI^+-MS m/z (relative intensity): 160 (72), 145 (82), 142 (20), 131 (100), 117 (27), 115 (36); Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46, H, 7.55, found C, 82.49, H, 7.51. The *ee* of 88% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK AD, heptane/*i*-PrOH 99/1, flow: 1 ml/min, λ = 254), retention times were 33.5 min (major) and 35.8 min.

(-)-(*1S, 2R*)-2-Isopropyl-1,2-dihydronaphth-1-ol (3c).



The reaction was carried out at –15°C, following the general procedure, employing chiral ligand **2** (37.73 mg, 0.07 mmol), substrate **1** (144 mg, 1.0 mmol) and *i*-Pr_2Zn (2.0 ml); conversion of the starting material (>98%) was reached within 26h. Purification by column chromatography (SiO_2, 10% AcOEt in hexanes) gave **3c** (103 mg, 55%) as an oil; R_f = 0.28 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = - 208.2° (c = 0.50, $CHCl_3$); IR (neat) 3391, 3034, 2960, 2928, 2874, 1635, 1458, 1384, 1368, 1265, 1033, 827 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (1H, d, *J* = 6.9 Hz), 7.31-7.18 (2H, m), 7.11 (1H, d, *J* = 7.7 Hz), 6.55 (1H, d, *J* = 9.5 Hz), 5.97 (1H, dd, *J* = 9.5, 4.8 Hz), 4.65 (1H, dd, *J* = 6.6, 4.4 Hz), 2.46-2.38 (1H, m), 1.74 (1H, dq, *J* = 13.5, 6.6 Hz), 1.63 (1H, d, *J* = 6.6 Hz, *OH*), 0.88 (3H, d, *J* = 6.6 Hz), 0.80 (3H, d, *J* = 6.9 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 136.4 ,128.8, 128.4, 127.7, 127.5, 126.8, 126.7, 126.5, 70.8, 41.9, 29.8, 20.7, 19.3; HRMS calcd. for $C_{13}H_{16}O$ $(M)^+$ 189.128, found 189.127. The *ee* of 91% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK OD, heptane/*i*-PrOH 99/1, flow: 1 ml/min, λ = 254), retention times were 26.1 min (major) and 35.8 min.

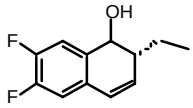
(-)-(*1S, 2R*)-2-*n*-Butyl-1,2-dihydronaphth-1-ol (3d).



The reaction was carried out following the general procedure employing chiral ligand **5** (42.10 mg, 0.07 mmol), substrate **1** (144 mg, 1.0 mmol) and *n*-But_2Zn (2.0 ml); conversion of the starting material (>98%) was reached within 68h. Purification by column chromatography (SiO_2, 10% AcOEt in hexanes) gave **3d** (192 mg, 95%) as a white solid. M.p. = 66°-67°C; R_f = 0.31 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -233.03° (c = 0.94, $CHCl_3$); IR (nujol) 3228, 3043, 2930,1927, 1610, 1458, 1260, 1025, 792 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (1H, d, *J* = 6.6 Hz), 7.26-7.14 (2H, m), 7.05 (1H, d, *J* = 6.6 Hz), 6.44 (1H, d, *J* = 9.5 Hz), 5.98 (1H, dd, *J* = 9.5, 4.8 Hz), 4.46 (1H, d, *J* = 4.8 Hz), 2.55-2.46 (1H, m), 1.76 (1H, *OH*), 1.42-1.18 (6H, m), 0.83 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.6, 132.3, 131.01, 128.4, 127.8, 127.5, 126.4, 125.8, 72.3, 42.4, 31.3, 29.2, 22.8, 13.9; EI^+-MS m/z (relative intensity): 202 (35), 173 (33), 145 (100), 141 (23), 127 (24), 117 (25); Anal. Calcd. for $C_{14}H_{18}O$: C, 83.12, H, 8.97, found C, 83.09, H, 8.93. The *ee* of 92% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK OD, heptane/*i*-PrOH 99/1, flow: 1 ml/min, λ = 254), retention times were 24.2 min (major) and 30.7 min.

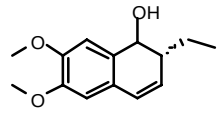
[2] Jeffrey, A.M.; Yeh, H.J.C.; Jerina, D.M.; de Marinis, R.M.; Foster, C.H.; Piccolo, D.E.; Berchtold, G.A. *J. Am. Chem. Soc.* **1974**, *96*, 6929

(-)-(*1S, 2R*)-2-Ethyl-6,7-difluoro-1,2-dihydronaphth-1-ol (11).



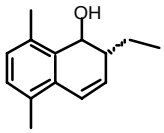
The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), 6,7-difluoro-1,4-epoxy-1,4-dihydronaphthalene (**6**)[3] (180 mg, 1.0 mmol) and Et_2Zn (1.82 ml); conversion of the starting material (75%) was reached within 70h. Purification by column chromatography (SiO_2, 10% AcOEt in hexanes) gave **11** (122 mg, 58%) as a white solid. M.p. = 54°-55°C (uncrist.); R_f = 0.31 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -125.7° (c = 1.19, $CHCl_3$); IR (nujol) 3274, 3061, 2965, 1633, 1599, 1498, 1311, 1263, 1082, 782 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19 (1H, dd, *J* = 10.6, 8.1 Hz), 6.88 (1H, dd, *J* = 10.6, 7.7 Hz), 6.37 (1H, d, *J* = 9.5 Hz), 5.99 (1H, dd, *J* = 9.5, 4.4 Hz), 4.46 (1H, d, *J* = 5.12 Hz), 2.48-2.37 (1H, m), 1.90 (1H, *OH*), 1.56-1.41 (1H, m), 1.39-1.26 (1H, m), 0.94 (3H, t, *J* = 7.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.8, 131.3, 124.6, 118.4, 116.6, 116.4, 115.1, 114.8, 71.2, 43.6, 24.2, 11.2; HRMS calcd. for $C_{12}H_{12}OF_2$ $(M)^+$ 210.085, found 210.084. The *ee* of 80% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK AD, heptane/*i*-PrOH 99/1, flow: 1 ml/min, λ = 254), retention times were 8.8 min (major) and 10.5 min.

(-)-(*1S, 2R*)-2-Ethyl-6,7-dimethoxy-1,2-dihydronaphth-1-ol (12).



The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), 6,7-dimethoxy-1,4-epoxy-1,4-dihydronaphthalene (**7**)[4] (204 mg, 1.0 mmol) and Et_2Zn (1.82 ml); conversion of the starting material (100%) was reached within 70h. Purification by column chromatography (SiO_2, 1% Et_3N, 15% AcOEt in hexanes) gave **12** (152 mg, 65%) as a solid. M.p. = 105-108°C (uncrist.). IR (neat) 3489, 3032, 2960, 2931, 1604, 1510, 1460, 1273, 1222, 1022, 860 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.89 (1H, s), 6.62 (1H, s), 6.38 (1H, d, *J* = 9.8 Hz), 5.90 (1H, dd, *J* = 9.8, 4.9 Hz), 4.45 (1H, d, *J* = 4.4 Hz), 3.89 (3H, s), 3.87 (3H, s), 2.51-2.36 (1H, m), 1.66 (1H, *OH*), 1.51-1.17 (2H, m), 0.94 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.8, 148.3, 128.7, 128.4, 125.5, 125.4, 111.5, 110.0, 72.2, 56.1, 44.3, 24.7, 11.6 ; HRMS calcd. for $C_{14}H_{18}O_3$ $(M)^+$ 234.125, found 234.126.

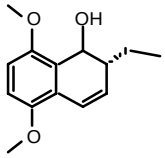
(-)-(*1S, 2R*)-2-Ethyl-5,8-dimethyl-1,2-dihydronaphth-1-ol (13).



The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), 5,8-dimethyl-1,4-epoxy-1,4-dihydronaphthalene (**8**)[5] (172 mg, 1.0 mmol) and Et_2Zn (1.82 ml); conversion of the starting material (>98%) was reached within 16h. Purification by column chromatography (SiO_2, 10% AcOEt in hexanes) gave **13** (182 mg, 90%) as an oil; R_f = 0.29 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -256.16° (c = 2.66, $CHCl_3$); IR (neat) 3348, 3049, 2960, 1464, 1375, 1257, 1165, 1047, 794 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.97 (2H, ABdd, *J* = 7.7 Hz), 6.69 (1H, d, *J* = 9.8 Hz), 6.08 (1H, dd, *J* = 9.8, 5.9 Hz), 4.75 (1H, br. singl.), 2.56-2.48 (1H, m), 2.37 (3H, s), 2.31 (3H, s), 1.76 (1H, *OH*), 1.29-1.19 (2H, m), 0.93 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.2, 132.7, 131.4, 130.1, 130.0, 129.9, 129.4, 122.7, 67.8, 43.7, 24.8, 18.9, 18.2, 12.1; HRMS calcd. for $C_{14}H_{18}O$ $(M)^+$ 202.1357, found 202.1356. The *ee* of >99% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK AD, heptane/*i*-PrOH 99/1, flow: 1 ml/min, λ = 254), retention times were 17.8 min (major) and 20.38 min.

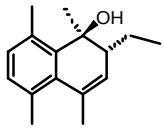
[3] Coe, P.L.; Waring, A.J.; Yarwood, T.D. *J. Chem. Soc. Perkin Trans. 1*, **1995**, 2729
[4] Giles, R.G.F.; Hughes, A.B.; Sargent, M.V. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 1581
[5] Jung, K.; Koreeda, M. *J. Org. Chem.* **1989**, *54*, 5667

(-)-(*1S, 2R*)-2-Ethyl-5,8-dimethoxy-1,2-dihydronaphth-1-ol (14).



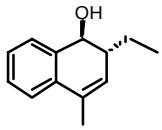
The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), 5,8-dimethoxy-1,4-epoxy-1,4-dihydronaphthalene (**9**)[6] (204 mg, 1.0 mmol) and Et_2Zn (1.82 ml); conversion of the starting material (>98%) was reached within 48h. Purification by column chromatography (SiO_2, 15% AcOEt in hexanes) gave **14** (192 mg, 82%) as an oil; R_f = 0.14 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -192.47° (c = 3.82, $CHCl_3$); IR (neat) 3431, 3045, 2960, 2837, 1599, 1487, 1450, 1381, 1263, 1087, 787 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.84 (1H, d, *J* = 9.9 Hz), 6.74 (2H, ABdd, *J* = 9.2 Hz), 6.06 (1H, dd, *J* = 9.9, 5.5 Hz), 4.96 (1H, br. singl.), 3.81 (3H, s), 3.78 (3H, s), 2.56-2.46 (1H, m), 2.12 (1H, *OH*), 1.28 (2H, dq, *J* = 13.2, 7.3 Hz), 0.92 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.3, 149.4, 130.3, 123.9, 122.1, 119.1, 110.9, 110.1, 64.9, 56.1, 55.9, 43.0, 25.3, 11.8; HRMS calcd. for $C_{14}H_{18}O_3$ $(M)^+$ 234.125, found 234.126. The *ee* of 97% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK OD, heptane/*i*-PrOH 90/10, flow: 1 ml/min, λ = 254), retention times were 10.6 min and 22.3 min (major).

(-)-(*1S, 2R*)-2-Ethyl-1,4-dimethyl-1,2-dihydronaphth-1-ol (15).



The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), 1,4-dimethyl-1,4-epoxy-1,4-dihydronaphthalene (**10**)[7] (172 mg, 1.0 mmol) and Et_2Zn (1.82 ml); conversion of the starting material (>98%) was reached within 40h. Purification by column chromatography (SiO_2, 10% AcOEt in hexanes) gave **15** (172 mg, 85%) as an oil; R_f = 0.4 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -31.03° (c = 2.03, $CHCl_3$); IR (neat) 3402, 3067, 3032, 2966, 2879, 1633, 1452, 1381, 1234, 1130, 1076, 783 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62-7.54 (1H, m), 7.29-7.18 (3H, m), 5.72 (1H, br. singl.), 2.29-2.20 (1H, m), 2.07 (3H, s), 1.87-1.75 (2H, m), 1.82 (1H, *OH*), 1.34-1.19 (1H, m), 1.27 (3H, s), 0.98 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.7, 133.9, 131.4, 127.8, 127.6, 127.2, 123.2, 123.1, 74.7, 48.5, 22.4, 21.0, 19.1, 12.1 ; HRMS calcd. for $C_{14}H_{18}O$ $(M)^+$ 202.1358 found 202.1364. The *ee* of 92% was determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK AD, heptane/*i*-PrOH 99/1, flow: 1 ml/min, λ = 254), retention times were 15.8 min (major) and 26.4 min.

(-)-(*1S,2R*)-2-Ethyl-4-methyl-1,2-dihydronaphth-1-ol (17).

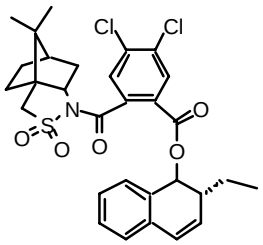


The reaction was carried out following the general procedure employing chiral ligand **2** (37.73 mg, 0.07 mmol), (±)-1-methyl-1,4-epoxy-1,4-dihydronaphthalene (**16**) (158 mg, 1.0 mmol) and Et_2Zn (0.68 ml, 0.75 eq.); conversion of the starting material (56%) was reached within 60h. Purification by column chromatography (SiO_2, 5% AcOEt in hexanes) gave **16** (52 mg, 33%) and **17** (74 mg, 39%) as a solid; M.p. = 48-50°C (uncrist.). ^1H NMR (200 MHz, $CDCl_3$) δ 7.41-7.20 (m, 4H), 5.80 (d, 1H, *J* = 6.13 Hz), 4.49 (dd, 1H, *J* = 7.08 and 6.13 Hz), 2.50-2.35 (m, 1H), 2.09 (s, 3H), 1.59-1.21 (m, 2H), 0.95 (t, 3H, *J* = 7.37 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 136.6, 134.0, 130.7, 128.2, 127.3, 123.3, 72.5, 43.9, 24.6, 19.1, 11.5; Anal. Calcd. for $C_{13}H_{16}O$: C, 82.94, H, 8.57, found C, 82.88, H, 8.65. The *ee* of 92%(**16**) and 86%(**17**) ware determined by HPLC on chiral stationary phase (DAICEL CHIRALPAK OD-H, heptane/*i*-PrOH 99/1, flow: 0,5 ml/min, λ = 254), retention times for compound **16** were 17.5 min (major) and 19.1 min; retention times for compound **17** were 22.4 min (major) and 24.7 min.

[6] Cragg, G.M.L.; Giles, R.G.F.; Roos, G.H.P. *J. Chem. Soc. Perkin Trans. 1*, **1975**, 1339
[7] Newman, M.S.; Dali, H.M.; Hung, W.M. *J. Org. Chem.* **1975**, *40*, 262

General procedure for the synthesis of racemic S_N2' *anti*-adducts: To a stirring suspension of CuCN (9.0 mg, 0.1 mmol) in anhydrous Et_2O (0.5 mL), at -40°C, was added dropwise the Grignard reagent (2.5 eq). The heterogeneous mixture was allowed to stir for 30 min at the same temperature and was then cooled down to -65°C. A solution of the oxabicyclic compound (0.5 mmol) in Et_2O (0.5 ml) was slowly added and the resulting mixture was allowed to warm up to r.t. The reaction was followed with analytical TLC and quenched, after complete conversion of the starting material, with saturated aqueous NH_4Cl. Extraction with Et_2O and evaporation of the dried ($MgSO_4$) organic phase gave almost exclusively the corresponding racemic S_N2' *anti*-adducts for all the oxabenzonorbornadiene substrates.

Synthesis of the sultam-ester (*1S, 2R*)



In a dry, three necked round-bottomed flask, at r.t., to a solution of (1*S*, 2*R*)-2-ethyl-1,2-dihydronaphth-1-ol (**3a**) (87 mg, 0.5 mmol) in dry CH_2Cl_2 (6 ml) was added, under vigorous stirring, the chiral auxiliary[8] (540 mg, 1.25 mmol). After 5 min, was added dicyclohexylcarbodiimmide (DCC, 257 mg, 1.25 mmol) and subsequently 4-dimethylamminopyridine (DMAP, 15 mg, 0.125 mmol). The mixture was left at reflux until complete conversion of the alcohol (checked by analytical TLC hex/AcOEt 85/15); the insoluble was filtered off by a short column of silica gel (CH_2Cl_2 as eluent). Purification by column chromatography (SiO_2, 15% AcOEt in hexanes) gave the title compound (256 mg, 87%) as a white solid. After recrystalization from methanol a suitable crystal for X-ray analysis was obtained. R_f = 0.286 on silica gel (hexanes/AcOEt 85/15); $[\alpha]_D^{20}$ = -203.63° (c = 1.24, $CHCl_3$); IR (nujol) 3095, 3072, 2960, 2731, 1745, 1718, 1703, 1680, 1666, 1585, 1552, 1375, 1255, 1145, 1120, 1087, 794 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (1H, s), 7.46 (1H, s), 7.35-7.10 (4H, m), 6.54 (1H, d, *J* = 9.89 Hz), 6.03 (1H, dd, *J* = 9.89, 5.13 Hz), 5.99 (1H, d, *J* = 2.93 Hz), 3.97-3.90 (1H, m), 3.39 (2H, ABdd, *J* = 13.92), 2.66-2.57 (1H, m), 2.54-2.42 (1H, m), 2.20-2.08 (1H, m), 1.98-1.84 (3H, m), 1.52-1.28 (4H, m), 1.24 (3H, s), 0.97 (3H, s), 0.94 (3H, t, *J* = 7.32 Hz); ^{13}C NMR (75 MHz,$CDCl_3$):δ 165.2, 162.9, 136.5, 134.6, 133.6, 131.4, 131.0, 130.4, 129.9, 129.7, 129.3, 128.9, 127.4, 126.4, 125.8, 74.9, 65.6, 52.9, 48.3, 47.7, 44.7, 40.8, 37.5, 33.0, 26.4, 20.8, 20.1, 11.4; TOF-MS m/z (relative intensity): 610 (63), 605 (25). Crystal data ($C_{30}H_{31}Cl_2NO_5S$), Mr=588.53, orthorhombic, colorless, platelet, $P2_12_12_1$, *a*=10.4788(4), *b*=24.743(1), *c*=11.0878(5) Å, *V*=2874.8(2) $Å^3$, *Z*=4, D_x=1.360 gcm^{-3}, F(000)=1232, μ=3.39 cm^{-1}, λ(Mo$K^-\alpha$)=0.71073 Å, T=100 K, *GooF*=1.045, *w*R(F^2)=0.0741 for 7631 reflections and 476 parameters and *R*(*F*)=0.0294 for 7283 reflections obeying F_o• 4.0 σ(F_o) criterion of observability.

[8] Harada, N.; Koumura, N.; Robillard, M. *Enantiomer* **1997**, *2*, 303